REMARKS

Reconsideration and allowance are respectfully requested.

Claims 47-52 and 91-102 are pending.

The amendments are supported by the original disclosure and, thus, no new matter has been added. If the Examiner should disagree, however, he is respectfully requested to point out the challenged limitation with particularity in the next Action so support may be cited in response.

Substitute paper and computer readable forms of the Sequence Listing are being submitted herewith in response to the Examiner's requirement. The paper and computer readable forms of the Sequence Listing do not add new matter, and their contents are the same. It is respectfully submitted that this submission complies with 37 CFR § 1.821 et seq. Otherwise, prompt notice of any defects in the Sequence Listing is earnestly solicited and additional time is requested to comply.

35 U.S.C. 112 – Definiteness

Claims 47, 49-50, 95 and 97 were rejected under Section 112, second paragraph, as being allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicants traverse.

The same amino acid sequence has been designated by two different sequence identifiers. This redundancy does not render the claims indefinite. But to advance prosecution in this application, the redundant sequence has been deleted and subsequent sequences have been renumbered. Substitute paper and computer readable forms of the Sequence Listing have been submitted herewith.

Typographical errors in the claims (e.g., capitalization, punctuation) have also been corrected. Such amendments also do not affect the scope of the claims and are being entered to address informalities.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 102 – Novelty

Claims 47-48 and 95-96 were rejected under Section 102(b) or (e) as allegedly being anticipated by Rosenthal et al. (WO 95/24213 or U.S. Patent 5,631,219). Applicants traverse.

The claim amendments are intended to overcome the anticipation rejection set forth in the Office Action. Hemoglobin contains four peptide chains and four heme groups. Stryer et al., *Biochemistry 2nd Ed.*, Freeman (New York, 1981) Chapter 3, pp. 43-63 (see enclosed). New independent claims 100 and 102 utilize the transitional phrase "consisting essentially of" which excludes the heme group. Therefore, it also excludes hemoglobin which contains heme groups.

Rosenthal et al. does not anticipate the claimed invention because all limitations of the independent claims 47 and 95 are not found in the cited reference. Moreover, the claims depending from the independent claims are also not anticipated by the reference because the limitations of claim 47 or 95 are incorporated in the dependent claims. See *In re McCarn*, 101 USPQ 411, 413 (C.C.P.A. 1954).

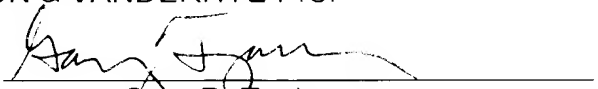
Withdrawal of the Section 102 rejection is requested.

Conclusion

Having fully responded to all of the pending objection and rejections of the Office Action (Paper No. 32), Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 

Gary R. Tanigawa
Reg. No. 43,180

1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

APPENDIX
MARKED-UP VERSION TO SHOW CHANGES

IN THE SPECIFICATION

The specification is amended as follows.

Page 24, third paragraph,

The invention also includes a method of inhibiting or stimulating stem cell proliferation comprising contacting hematopoietic cells with a peptide selected from the group of hemorphin peptides having the sequence:
Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO:4),
Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO:5),
Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:6),
Leu-Val-Val-Tyr-Pro-Trp-Thr (SEQ ID NO:7),
Leu-Val-Val-Tyr-Pro-Trp (SEQ ID NO:8),
Leu-Val-Val-Tyr-Pro (SEQ ID NO 9),
Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:10),
Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO:11),
Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO:12),
Tyr-Pro-Trp-Thr-Gln (SEQ ID NO 13), and
Tyr-Pro-Trp-Thr (SEQ ID NO:27) [(SEQ ID NO:28)].

Page 25, second paragraph,

The invention also includes a method of inhibiting or stimulating stem cell proliferation comprising contacting hematopoietic cells with a peptide selected from the group consisting of Tyr-MIF- 1 related peptides, casomorphins, cytochrophins and exorphins. Specifically included are the Tyr-MIF-1 peptides having the sequences:
Tyr-Pro-Try-Gly-NH_2 (SEQ ID NO:28) [(SEQ ID NO:29)],
Tyr-Pro-Lys-Gly-NH_2 (SEQ ID NO:29) [(SEQ ID NO:30)],
Tyr-Pro-Leu-Gly-NH_2 (SEQ ID NO:30) [(SEQ ID NO:31)], and
Pro-Leu-Gly-NH_2.

Pages 25-26, third paragraph,

The invention also includes a method of inhibiting or stimulating stem cell proliferation comprising contacting hematopoietic cells with an opiate peptide selected from the group consisting of

(D-Ala^2,N-Me-Phe^4,Gly-ol^5)-Enkephalin (DAMGO),

(D-Arg^2,Lys^4)-Dermorphin-(1-4)-amide (DALDA),

(Phe^4)-Dermorphine (1-4) amide

Ac-Arg-Phe-Met-Trp-Met-Arg-NH_2 (SEQ ID NO:14),

Ac-Arg-Phe-Met-Trp-Met-Lys-NH_2 (SEQ ID NO:31) [(SEQ ID NO:32)], and

H-Tyr-Gly-Gly-Phe-Met-Arg-Arg-Val-NH_2 (SEQ ID NO:32) [(SEQ ID NO:33)].

Page 82, third paragraph,

Two hemorphin sequences, hemorphin 10 (amino acids 32-41 of the beta chain sequence) and hemorphin 7 (amino acids 33-40) were tested and found to be active. The sequences are as follows:

Hermorphin 10 Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO:4) [(SEQ ID NO:26)]

Hemorphin 7 Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO:26) [(SEQ ID NO:27)]

IN THE CLAIMS

The claims are amended as follows.

47. (3 x Amended) A method of stimulating stem cell proliferation comprising contacting hematopoietic cells with a stem cell proliferation stimulating amount of INPROL or an opiate compound or a stem cell proliferation stimulating amount of a combination of INPROL and an opiate compound,

wherein said INPROL is selected from the group consisting of [the alpha chain of hemoglobin, the beta chain of hemoglobin, the gamma chain of hemoglobin, the delta chain of hemoglobin, the epsilon chain of hemoglobin, the zeta chain of hemoglobin,]

a polypeptide having the sequence of amino acids 1-97 of the human alpha hemoglobin chain,

a polypeptide having the sequence of amino acids 1-94 of the human alpha hemoglobin chain,

Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val[,] (SEQ ID NO:1),

Cys-Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val-Cys (SEQ ID NO:2)

(where the two Cys residues form a disulfide bond),

Asp-Ala-Leu-Thr-Asn[asn]-Ala-Val-Ala-His-Val-Asp-Asp-Met-Pro-Asn-Ala[ala]-Leu-Ser-Ala (SEQ ID NO:3),

Phe-Leu-Gly-Phe-Pro-Thr (SEQ ID NO: 33), [(SEQ ID NO:34),]

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO:4),

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO:5),

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:6),

Leu-Val-Val-Tyr-Pro-Trp-Thr (SEQ ID NO:7),

Leu-Val-Val-Tyr-Pro-Trp (SEQ ID NO:8),

Leu-Val-Val-Tyr-Pro (SEQ ID NO:9),

Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:10),

Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO:11),

Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO:12),

Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:13), and

Tyr-Pro-Trp-Thr (SEQ ID NO:27); [(SEQ ID NO:28),]

wherein said stem cells are cells which can generate multiple lineages or other stem cells.

48. (2 x Amended) A method as in claim 47 wherein said INPROL is selected from the group consisting of [the alpha chain of hemoglobin, the beta chain of hemoglobin, the gamma chain of hemoglobin, the delta chain of hemoglobin, the epsilon chain of hemoglobin, the zeta chain of hemoglobin,]

a polypeptide having the sequence of amino acids 1-97 of the human alpha hemoglobin chain, and

a polypeptide having the sequence of amino acids 1-94 of the human alpha hemoglobin chain.

49. (3 x Amended) A method as in claim 47 wherein said INPROL is selected from the group consisting of peptides having the sequence:
Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val[,] (SEQ ID NO:1),
Cys-Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val-Cys (SEQ ID NO:2)
(where the two Cys residues form a disulfide bond),
Asp-Ala-Leu-Thr-Asn-Ala-Val-Ala-His-Val-Asp-Asp-Met-Pro-Asn-Ala[ala]-Leu-Ser-Ala (SEQ ID NO:3),
Phe-Leu-Gly-Phe-Pro-Thr (SEQ ID NO:33), [(SEQ ID NO:34),]
Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO:4),
Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO:5),
Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:6),
Leu-Val-Val-Tyr-Pro-Trp-Thr (SEQ ID NO:7),
Leu-Val-Val-Tyr-Pro-Trp (SEQ ID NO:8),
Leu-Val-Val-Tyr-Pro (SEQ ID NO:9),
Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:10),
Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO:11),
Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO:12),
Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:13), and
Tyr-Pro-Trp-Thr (SEQ ID NO:27) [(SEQ ID NO:28)].

50. (Amended) A method as in claim 47 wherein said opiate compound is selected from the group consisting of morphine, etorphine, codeine, heroin, hydromorphone, oxymorphone, levorphanol, levallorphain, [codeine,] hydrocodone, oxycodone, nalorphine, naloxone, buprenorphine, butanorphanol, nalbuphine, meperidine, alphaprodine, diphenoxylate, fentanyl, (D-Ala^2,N-Me-Phe^4,glycinol^5)-Enkephalin, (D-Arg^2,Lys^4)-Dermorphin (1-4) amide and nociceptin.

51. (2 x Amended) A method of stimulating stem cell proliferation comprising contacting hematopoietic cells with a stem cell proliferation stimulating amount of a compound capable of binding opiate receptors, wherein said stem cells are cells which can generate multiple lineages or other stem cells.

92. (Amended) The method of claim 49, comprising contacting hematopoietic cells with a stem cell proliferation stimulating amount of Cys-Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val-Cys[-] (SEQ ID NO:2) wherein the two Cys residues form a disulfide bond.

95. (2 x Amended) A method of stimulating stem cell proliferation comprising contacting stem cells with a stem cell proliferation stimulating amount of INPROL or an opiate compound or a stem cell proliferation stimulating amount of a combination of INPROL and an opiate compound,

wherein said INPROL is selected from the group consisting [of the alpha chain of hemoglobin, the beta chain of hemoglobin, the gamma chain of hemoglobin, the delta chain of hemoglobin, the epsilon chain of hemoglobin, the zeta chain of hemoglobin,]

a polypeptide having the sequence of amino acids 1-97 of the human alpha hemoglobin chain,

a polypeptide having the sequence of amino acids 1-94 of the human alpha hemoglobin chain,

Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val[,] (SEQ ID NO:1),

Cys-Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val-Cys (SEQ ID NO:2)

(where the two Cys residues form a disulfide bond),

Asp-Ala-Leu-Thr-Asn[asn]-Ala-Val-Ala-His-Val-Asp-Asp-Met-Pro-Asn-Ala[ala]-Leu-Ser-Ala (SEQ ID NO:3),

Phe-Leu-Gly-Phe-Pro-Thr (SEQ ID NO:33), [(SEQ ID NO:34),]

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO:4),

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO:5),

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:6),

Leu-Val-Val-Tyr-Pro-Trp-Thr (SEQ ID NO:7),

Leu-Val-Val-Tyr-Pro-Trp (SEQ ID NO:8),

Leu-Val-Val-Tyr-Pro (SEQ ID NO:9),

Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:10),

Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO:11),

Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO:12),

Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:13), and

Tyr-Pro-Trp-Thr (SEQ ID NO:27); [(SEQ ID NO:28),]

wherein said stem cells are cells which can generate multiple lineages or other stem cells.

96. A method as in claim 95 wherein said INPROL is selected from the group consisting of [the alpha chain of hemoglobin, the beta chain of hemoglobin, the gamma chain of hemoglobin, the delta chain of hemoglobin, the epsilon chain of hemoglobin, the zeta chain of hemoglobin,]

a polypeptide having the sequence of amino acids 1-97 of the human alpha hemoglobin chain, and

a polypeptide having the sequence of amino acids 1-94 of the human alpha hemoglobin chain.

97. (Amended) A method as in claim 95 wherein said INPROL is selected from the group consisting of peptides having the sequence:

Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val[,] (SEQ ID NO:1),

Cys-Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val-Cys (SEQ ID NO:2)

(where the two Cys residues form a disulfide bond),

Asp-Ala-Leu-Thr-Asn-Ala-Val-Ala-His-Val-Asp-Asp-Met-Pro-Asn-Ala[ala]-Leu-Ser-Ala (SEQ ID NO:3),

Phe-Leu-Gly-Phe-Pro-Thr (SEQ ID NO:33), [(SEQ ID NO:34),]

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO:4),

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO:5),

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:6),

Leu-Val-Val-Tyr-Pro-Trp-Thr (SEQ ID NO:7),

Leu-Val-Val-Tyr-Pro-Trp (SEQ ID NO:8),

Leu-Val-Val-Tyr-Pro (SEQ ID NO:9),

Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:10),

Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO:11),

Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO:12),

Tyr-Pro-Trp-Thr-Gln (SEQ ID NO:13), and
Tyr-Pro-Trp-Thr (SEQ ID NO:27) [(SEQ ID NO:28)].

Claims 100-102 have been added.

IN THE SEQUENCE LISTING

The substitute paper and computer readable copies of the Sequence Listing are attached.